

Borane-Catalyzed Ring-Opening and Ring-Closing Cascades of Furans Leading to Silicon-Functionalized Synthetic Intermediates

Nat. Commun. **2016**, *7*, 13431

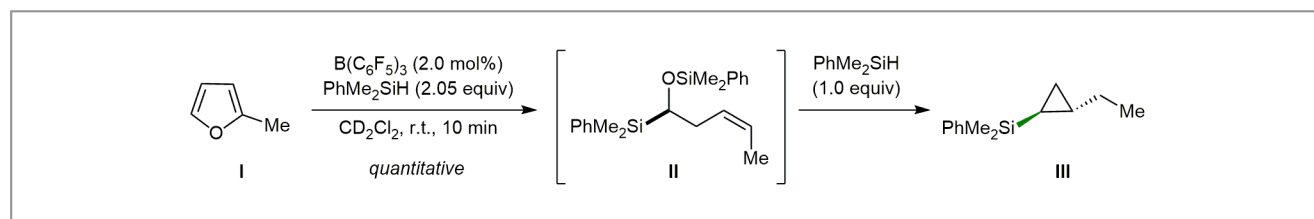
A number of transition-metal complexes are known to efficiently catalyze hydrosilylation of unsaturated functionalities including C=O, C=N and C=C bonds, largely via inner- or outer-sphere pathways. Representatively, a series of platinum-based hydrosilylation catalysts (e.g. Karstedt's catalyst) display powerful and selective catalytic performance, especially in hydrosilylation of alkenes, thus enabling large-scale synthesis of various alkyl silanes in industry. However, most of the presently available hydrosilylation processes rely on the use of expensive transition metals (Rh, Ir, Pt, or Pd). In this regard, certain Lewis acids such as $B(C_6F_5)_3$ have drawn significant attention as catalysts due to their practical merits. In 1996, the Piers group first reported the $B(C_6F_5)_3$ -catalyzed hydrosilylation of aromatic aldehydes, ketones, and esters (for references see the original *Nat. Commun.* article). Since then, the $B(C_6F_5)_3$ catalyst system has been shown to be effective not only for hydrosilylation of unsaturated functionalities but also for reductive sp^3 -C-X bond cleavage (X = O, S, or halides) using hydrosilanes. The Park and Chang group from the Institute for Basic Science and KAIST (Daejeon, South Korea) recently reported the $B(C_6F_5)_3$ -catalyzed dearomative silylative reduction of quinolines and pyridines leading to (partially) saturated azacyclic products having sp^3 -C-Si bonds *beta* to the nitrogen atom. Subsequently, they also showed that α,β -unsaturated nitriles and esters can undergo a selective silylative reduction.

Continuing their efforts along these lines, Professor Chang and co-workers turned their attention to furans, one of the representative biomass-derived chemicals, mainly due to the fact that furans are predicted to undergo reductive cleavage serving as various types of carbon sources. The Chang group envisioned that $B(C_6F_5)_3$ would be capable of catalyzing a hydrosilylative transformation of furans. Professor Chang

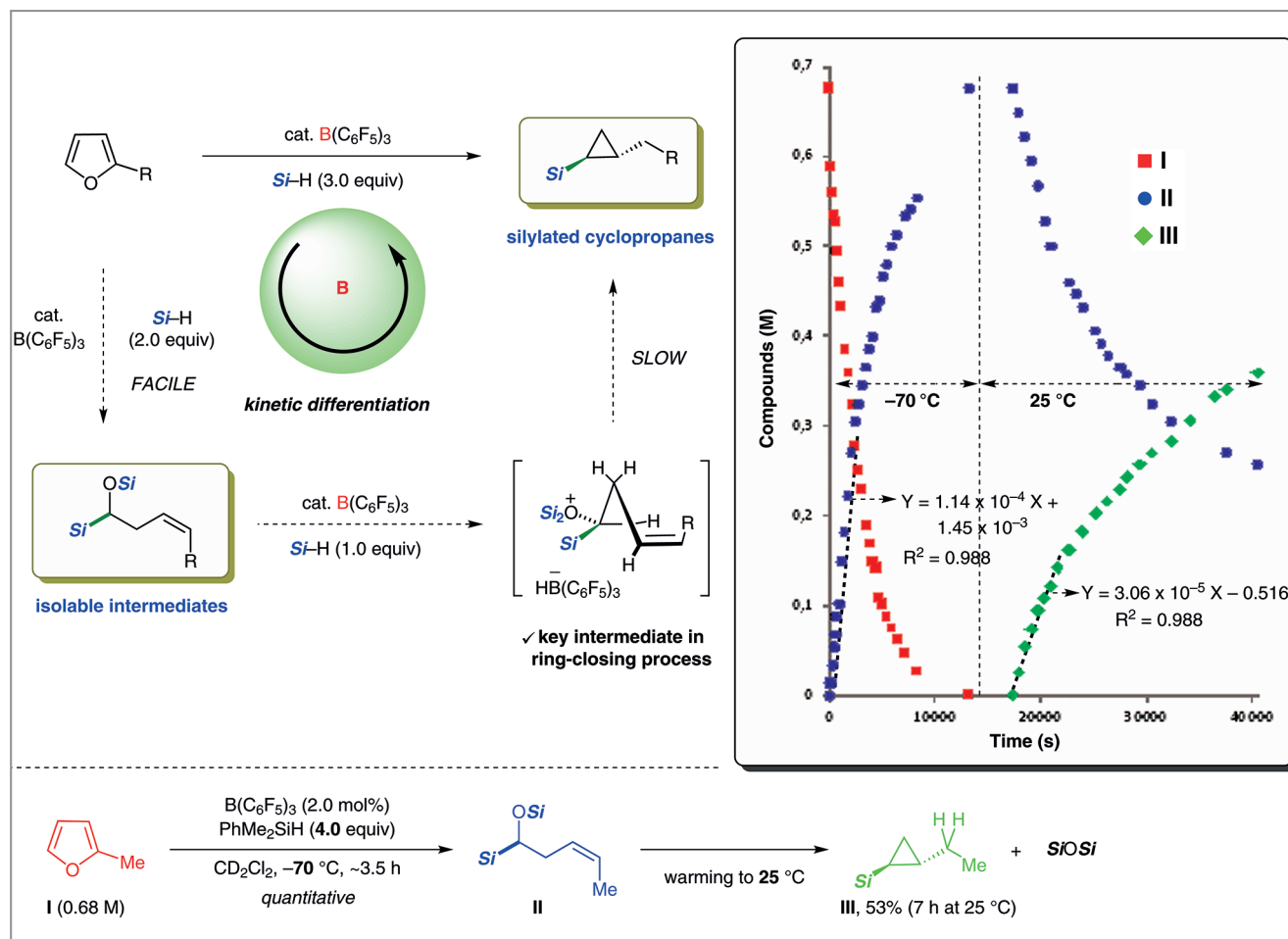
said: "The unique reactivity of $B(C_6F_5)_3$ /hydrosilane toward the sp^3 -C-O and sp^2 -C=C bonds initially made us curious about which products could be generated from furans under the $B(C_6F_5)_3$ -mediated hydrosilylation conditions." In a preliminary reaction, 2-methylfuran (**I**) was subjected to the $B(C_6F_5)_3$ -catalytic conditions to reveal that **I** underwent ring-opening with $PhMe_2SiH$, leading to the corresponding alkenyl silyl ether bearing an sp^3 -C-Si bond *alpha* to the oxygen atom (**II**). Interestingly, the double bond in the product was determined to be exclusively *Z*. "Such an unprecedented ring-opening product with excellent chemo-, regio-, and stereoselectivities under mild metal-free conditions is considered to be exceptional, and it also caught our attention with regard to the mechanistic pathway," remarked Professor Chang. Through a set of optimization studies, the authors found that as little as 2.0 mol% of $B(C_6F_5)_3$ with 2.05 equivalents of $PhMe_2SiH$ allowed for quantitative silylative ring opening of **I** at room temperature within ten minutes (Scheme 1).

"More interestingly, when one more equivalent of $PhMe_2SiH$ was added into the reaction mixture, we observed an exothermic reaction with a new product formation," said Professor Chang. He continued: "The structure of this new compound was identified to be a silylated cyclopropane (**III**) with exclusive *anti*-diastereoselectivity with the formation of a stoichiometric amount of disiloxane by-product."

To gain mechanistic insights, the Chang group conducted an NMR study in a reaction of 2-methylfuran (**I**) with $PhMe_2SiH$ (4.0 equiv, Scheme 2). "Low-temperature NMR monitoring was a useful analytical technique especially for a rapid cascade transformation as in this case," remarked Professor Chang. He continued: "The reaction was observed to proceed smoothly at $-70^\circ C$ leading to (*Z*)- α -silyloxy alkenyl



Scheme 1 $B(C_6F_5)_3$ -catalyzed silylative ring-opening and ring-closing cascade of 2-methylfuran (**I**)



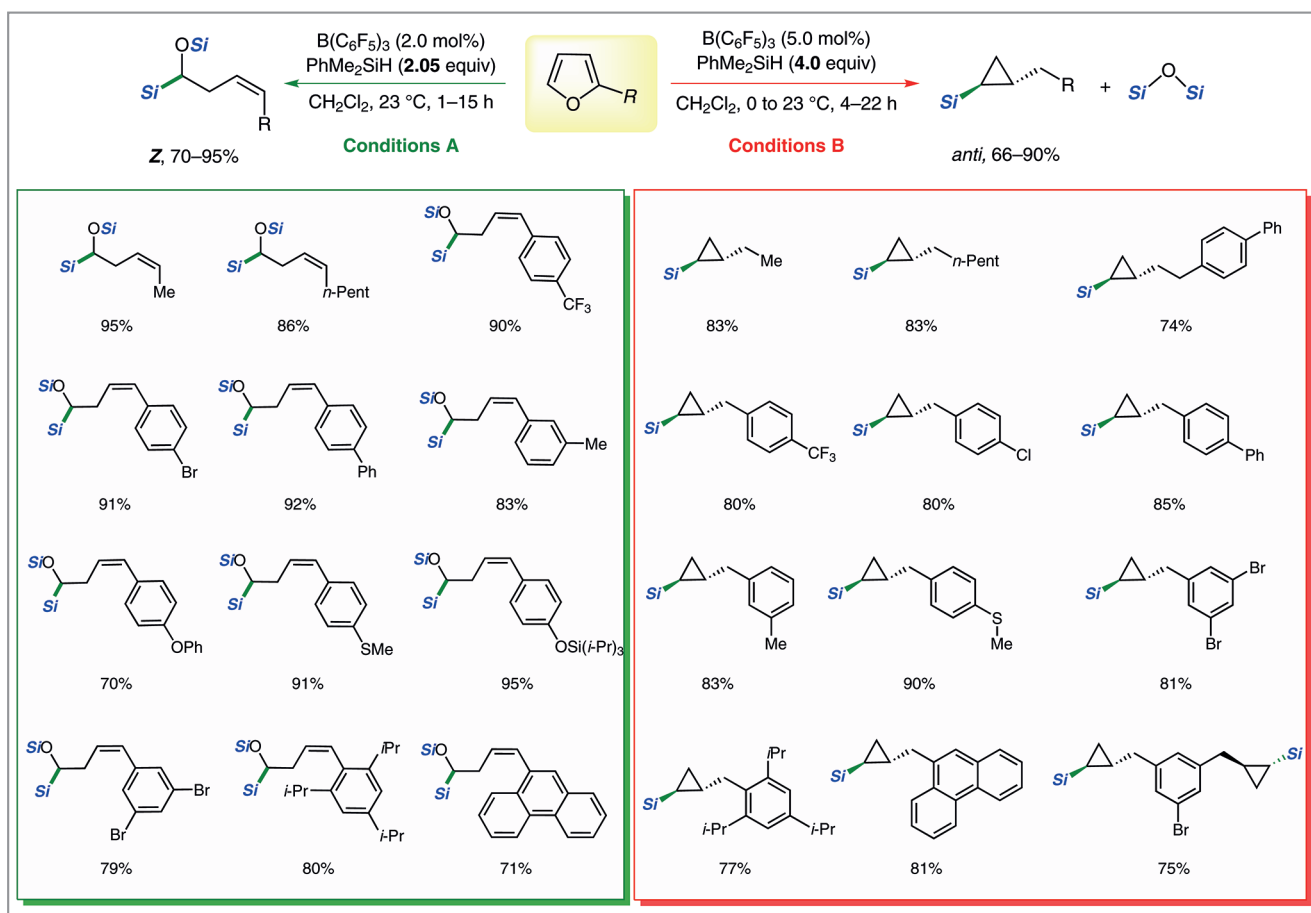
silane (**II**) quantitatively over 3.5 hours. Upon further warming to room temperature, the in situ generated intermediate **II** was converted into the corresponding silylated cyclopropane (**III**). These results clearly indicated that the ring-opening and ring-closing cascade of 2-methylfuran (**I**) proceeded under perfect kinetic differentiation."

With this mechanistic depiction, Chang and co-workers explored the substrate scope (Scheme 3). Professor Chang said: "We were pleased to see that a variety of 2-substituted furans were transformed into a single product of α -silyloxy-(*Z*)-homoallylsilanes in high yields under standard conditions with excellent stereoselectivity (*Z/E* > 99:1, Scheme 3; Conditions A)." Professor Chang also said: "In agreement with the kinetic behavior observed in the low-temperature NMR study, a range of 2-substituted furans were smoothly converted into *anti*-2-alkylcyclopropyl silanes at room temperature in good

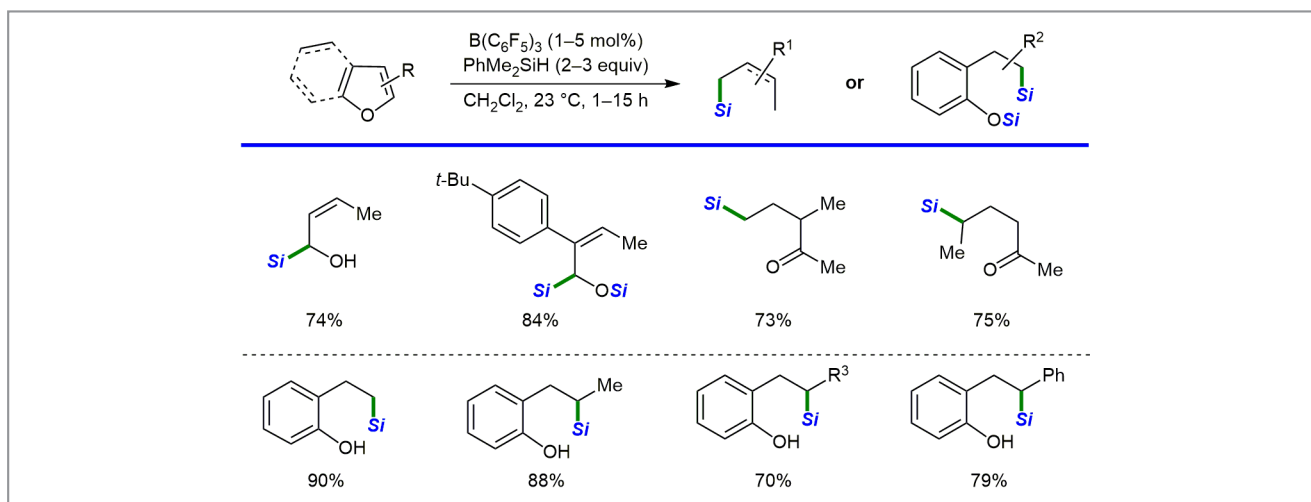
to high yields irrespective of their electronic and steric variations when PhMe_2SiH (4.0 equiv) was used in the presence of $\text{B}(\text{C}_6\text{F}_5)_3$ (5.0 mol%) catalyst (>99% *anti*-selectivity, Scheme 3; Conditions B)."

Subsequently, Professor Chang and co-workers found that the present $\text{B}(\text{C}_6\text{F}_5)_3$ catalysis was applicable for the silylative ring opening of additional furan derivatives, providing the corresponding silylated products in good yields (Scheme 4). "It is notable that the chemoselectivity was altered depending on the position of substituents on the furan substrates, thus delivering a range of various ring-opening products," remarked Professor Chang.

In addition, Professor Chang and co-workers demonstrated the synthetic utility of two types of products obtained through the present $\text{B}(\text{C}_6\text{F}_5)_3$ -catalyzed hydrosilylation cascade of furans (Scheme 5). Professor Chang explained: "The



Scheme 3 $\text{B(C}_6\text{F}_5)_3$ -catalyzed cascade silylative transformation of furans ($\text{Si} = \text{SiMe}_2\text{Ph}$)



Scheme 4 $\text{B(C}_6\text{F}_5)_3$ -catalyzed silylative ring opening of alkyl furans and benzofurans ($\text{Si} = \text{SiMe}_2\text{Ph}$, $\text{R}^3 = 4\text{-TIPSO-C}_6\text{H}_4$, TIPS = triisopropylsilyl)

obtained products of α -silyloxy homoallylsilanes and *anti*-2-alkylcyclopropyl silanes possess synthetic building units which are readily transformed into other synthetically valuable functional groups. Therefore, the synthetic utility of the present method could be potentially broad in synthetic and medicinal chemistry."

“In conclusion, chemodivergent catalytic transformations of furans have been developed to furnish synthetically valuable silicon-functionalized products, α -silyloxy-(*Z*)-alkenyl silanes and *anti*-cyclopropyl silanes with excellent diastereoselectivity,” said Professor Chang. He also noted: “The mechanistic pathway of this cascade reaction was well elucidated by a series of mechanistic experiments.” Finally, he commented: “The present procedure showcases an example of biomass conversion to provide synthetically valuable chemicals under extremely mild and convenient conditions without requiring transition-metal species.”

Matt's tank

About the authors



Dr. C. K. Hazra

Chinmoy Kumar Hazra is currently working as a postdoctoral scientist under Professor Sukbok Chang at the Institute for Basic Science (IBS) (South Korea). He obtained his Ph.D. from the Westfälische Wilhelms-Universität Münster (Germany) in 2013 (Professor Martin Oestreich) and his M.S. degree in chemistry from the Indian Institute of Technology Bombay (India) in 2010. He also stayed at the University of Strasbourg (France) for a postdoctoral experience with Professor Françoise Colobert. His research interests include the development of metal-free catalysis with mechanistic understanding and synthetic applications.



Dr. N. Gandhamsetty

Narasimhulu Gandhamsetty was born in 1980 and raised in Sathupalli (Kadapa, India). He obtained his Ph.D. at the Indian Institute of Chemical Technology (India) under Professor Jhillu S. Yadav in 2014. Currently, he is working as a postdoctoral scientist under Professor Sukbok Chang at the Institute for Basic Science (IBS) (South Korea). He received an 'outstanding research award' from IBS in 2016. His research interests are the development of new synthetic methods, silylative reductions, and organocatalytic methodologies for general applications in synthetic organic chemistry.



Dr. S. Park

Sehoon Park was born in Seoul (South Korea) in 1977 and received his Ph.D. (2008) in chemistry from the Tokyo Institute of Technology (Japan) under Professor Kohtaro Osakada, where he received a Monbukagakusho scholarship (2004–2008). He then joined the University of North Carolina at Chapel Hill (USA) as a postdoctoral fellow (Professor Maurice Brookhart, 2009–2012). In 2013, he joined Professor Chang's group at the Institute for Basic Science (IBS) (South Korea), where he is a senior research fellow. He was a recipient of the outstanding research award in 2014. Currently, he is also an Adjunct Professor at the Korea University of Science and Technology. His research interests are synthetic and mechanistic organometallic chemistry as well as synthetic methodology in catalysis.



Prof. S. Chang

Sukbok Chang is Director at the Center for Catalytic Hydrocarbon Functionalizations in a program of the Institute for Basic Science (IBS) (South Korea) and also Professor at the Korea Advanced Institute of Science & Technology (KAIST). In 1996, he earned his Ph.D. at Harvard University (USA) under Professor Eric N. Jacobsen. After postdoctoral work at Caltech (USA) with Professor Robert H. Grubbs, he joined Ewha Womans University in Seoul (South Korea) as an Assistant Professor in 1998, and moved to KAIST in 2002. His research interests include the development and mechanistic understanding of metal-catalyzed organic transformations.